REMARKS

Applicants note that the Office Action indicates on page 2 that the Action is "non-final." Page 6 of the Action, however, indicates the Action is "made final." In view of the confusion created by these inconsistent indications in the Action, Applicants telephoned the Examiner for clarification. In a phone call to Mr. Bradley Crawford on January 18, 2006, the Examiner stated that the Office had reviewed the Action and determined it should be considered non-final. Thus, Applicants are treating this response as a response to a non-final Action.

Claims 1-3, 4, 5, 9, 10, 12, 13, 19, 20 have been cancelled without prejudice to the filing of continuing applications.

Claims 14-18 have been withdrawn from further consideration pursuant to 37 C.F.R. §1.142(b).

New claims 23-24 have been added. These new claims replace cancelled claims 5, 10, 12 and 13. Claims 6, 7, 8, 11, 21 and 22 have been amended to properly depend from a pending claim.

The new claims are fully supported by the specification as originally filed. Thus, no new matter is added by the amendments herein.

Rejection under 35 USC §103

Claims 5-8 and 10-13 stand rejected under 35 USC § 103(a) as being unpatentable over Yanni et al., U.S. Patent No. 5,696,166, in view of Wollard, Prostaglandins 1989, Vol. 38(4) pages 465-471

and Herbertsson et al., J of Lipid Research, 1998 Vol 39, pages 237-244 for the reasons stated in the prior office action.

That rejection is respectfully traversed.

While admitting that Yanni did not per se teach inhibition of a fibroblast to an adipocyte, the Examiner urges that since 12-HETE is an arachidonic metabolite, one of ordinary skill in the art would have expected differentiation of a fibroblast to occur anyway because arachidonic acid metabolites inhibit adipocyte production which elicits inflammatory response via prostaglandin synthesis.

12-HETE actually is an arachidonic metabolite. However, 12-HETE is not the only arachidonic metabolite, PG52 being also an arachidonic metabolite.

Contrary to the Examiner's statement, not all of the various arachidonic metabolites inhibit differentiation of fibroblasts to adipocytes.

In particular, PG52 does not.

And, in any case, the Applicants have surprisingly found that only two particular arachidonic metabolites, i.e., 12-HETE and 11,12-EET, are capable of inhibiting the differentiation of fibroblasts to adipocytes.

Yanni does not disclose that particular property of 12-HETE.

Yanni et al. teach

- an ophthalmic composition

to be

- administered topically

which

- comprises an amount of 12-HETE optionally incorporated in a gel

and which is used

- in a method for treating dry eye disorders.

In new claims 23 and 24, it is emphasized that in the method of inhibiting differentiation of fibroblasts into adipocytes according to the invention, a composition comprising at least one of 12-HETE and 11,12-EET is administered

- as a nutriceutical formulation or
- topically on the areas concerned by localized excess subcutaneous fat deposits.

The composition according to Yanni is an ophthalmic composition that is administered topically for treating dry eye disorders (which, in the context of Yanni, means on the area of the eye).

Not only did Yanni not discover the capability of 12-HETE to inhibit differentiation of fibroblasts to adipocytes but moreover Yanni's composition did not inherently inhibit differentiation of fibroblasts because the area comprising the eye does not comprise localized excess subcutaneous fat deposits.

Consequently, the invention as defined in new claims 23 and 24 is patentable over Yanni and the rejection based on that reference cannot be sustained in view of the analysis presented above by the Applicants.

According to the Examiner, "Herbertsson et al. teach (on page 240, right hand side column underlined), of detection of 12(S)-HETE to other cells, and in the discussion section on page 242 teach the expression in pre-adipocytes which appears to inhibit differentiation to adipocytes as in claim 10.".

The Examiner's interpretation of Herbertsson et al. is respectfully traversed.

First of all, it is important to note that the claimed invention requires the use of 12-HETE and/or 11,12-EET in a method of inhibiting differentiation of pre-adiopocyte fibroblasts to adipocytes.

As pointed out above, Applicants have surprisingly discovered that two of the metabolites of arachidonic acid, 12-HETE and 11,12-EET have that capability.

And that property of the two metabolites in question was all the more surprising and unexpected as not only arachidonic acid from which they are metabolites but also at least one other metabolite, i.e. PGJ2, was well-known as promoting the differentiation of preadipocyte fibroblasts to adipocytes.

Contrary to the Examiner's analysis, the said property, i.e. the capability of inhibiting differentiation of preadipocyte fibroblasts to adipocytes was not obvious from Herbertsson et al.

Herbertsson et al. deal with the identification of the

- 650kDa 12(S)-HETE binding complex in carcinoma cells.

The passage on page 240 of Herbertsson et al. was already thoroughly analyzed by Applicants in the amendment filed on September 8, 2005. That passage is again set forth below.

> *"3T3-L1 preadipocytes bound approximately the same amount of 12(S)-HETE as Lewis lung carcinoma cells. When these cells had been differentiated to adipocytes, the "binding capacity was reduced about six times."*

The indisputable conclusion from these results is that under the conditions of the experiment referred to, preadipocytes differentiated to adipocytes, which means that from that disclosure, the skilled artisan could not deduce the capability of 12(S)-HETE of inhibiting the said differentiation.

With respect to the above-cited passage page 240 of Herbertsson et al., the Examiner's comments are ".... Herbertsson et al. used 5 different cell lines, 3T3-L1 binds approximately the same amount of 12(S)-HETE as lewis lung indicating that once the cells are differentiated to adipocytes the binding capability

was reduced, these cells were however used as a negative control as they do not produce 12(S)-HETE, further in the reference (page 240 left column, second paragraph, states that TNF-induced c-fos expression which appears to be dependent on formation of HETEs prevented differentiation to adipocytes.

Applicants agree that Herbertsson et al. used

"... five different cell lines..."

but with the purpose

"... to form a 650 kDa 12(S)-HETE binding complex".

among which however only one, i.e., 3T3-L1, consists of preadipocytes, but Applicants respectfully disagree with the Examiner's statement according to which

"These cells were however used as negative control".

Indeed, that latter comment of Herbertsson et al. concerns the

Intestine 407 cells

but not the

3T3-L1 cells.

And the only conclusion which can be drawn from the Examiner's following citation of Herbertsson et al., i.e.,

"... TNF-induced c-fos expression in preadipocytes which appears to be dependent on formation of HETES, prevented differentiation to adipocytes..."

is that it is

"The TNF-induced c-fos expression"

which prevents differentiation into adipocytes and not 12-HETE.

That conclusion is supported by the attached Rule 132 declaration of Philippe Potin, Ph.D.

Thus, the rejection based on Herbertsson et al. has been overcome by the above arguments.

In the last paragraph of page 4 of the Action, the Examiner urges that on page 242, right column, the Herbertsson et al. reference

> *"... clearly states the observed decrease in the amount of 12(S)-HETE binding couplers in differentiated 3T3-L1cell."*

But, from that statement, the property of the metabolite in question which renders the latter capable of inhibiting differentiation of fibroblasts into adipocytes is simply not obvious.

This point is discussed in the attached Potin Declaration.

Claims 6-8, 11, and 19-22 stand rejected under 35 US.C. 103(a) as being unpatentable over Herbertsson et al., J. of Lipid Research, 1998 Vol 39, pages 237-244 in view of Yanni et al., U.S. Patent No. 5,696,166.

That rejection is respectfully traversed.

According to the Examiner,

> *"Herbertsson teaches current claim 19 a method of inhibiting differentiation of*

fibroblast to adiposyte at page 242 (right hand col. second paragraph), wherein the metabolite is 12(S) current claim 2 (see abstract)."

Applicants disagree for the reasons set forth above with respect to the actual teaching of Herbertsson.

Again, according to the Examiner

- *"Yanni teaches current claim 6, wherein the composition of 12-HETE is administered in the forme of gel at col. 5 line 27, wherein one 12-HETE comprises of 12 ® (S) currents claims 7 and 8 at col. 9, line 50, and*
- *"It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to administer 12-HETE compositions- an arachidonic metabolite to treat human neutrophils and for cell survival. These compounds are known in the art to bind to human leukemia cell and murine pre-adipocytes by blocking specific 12S or 12R receptors."*

Applicants respectfully submit that the claimed use of the two metabolites 12-HETE and 11,12-EET is not rendered obvious by these statements.

The Examiner then states that

> *"One of ordinary skill in the art would have been motivated to combine the teachings of Herbertsson with that of Yanni, used either 12(S) or 12® to inhibit differentiation of fibroblast to adipocyte as both enatiomers are metabolites of the arachidonic acid and has both been used in the prior art, therefore would have expected successfully result in doing so.".*

One of ordinary skill in the art would not combine the teachings of Herbertsson with those of Yanni.

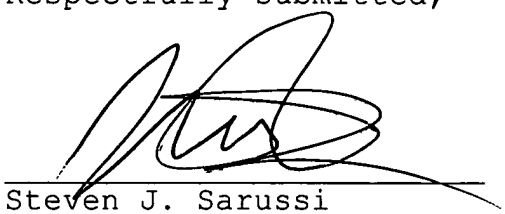
This position is supported by the attached Potin Declaration.

Applicants respectfully submit that the above arguments overcome the rejection under 35 U.S.C. §103. Reconsideration and withdrawal of the rejection is solicited.

In view of the above amendments and remarks, Applicants respectfully submit that the claims are in condition for allowance. A Notice of Allowance is therefore respectfully solicited.

The Applicants urge the Examiner to contact the Applicants' undersigned representative at (312) 913-2136 if he believes that a discussion would expedite prosecution of this application.

Respectfully submitted,

Dated: January 20, 2006 By: 

Steven J. Sarussi
Reg. No. 32,784

McDonnell Boehnen
Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, Illinois 60606
(312) 913-0001